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10/501,675	07/16/2004	Yuji Imai	IMAI13	5140

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EXAMINER	
WALICKA, MALGORZATA A	
ART UNIT	**PAPER NUMBER**
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,675	IMAI ET AL.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Nov. 11, 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 23-30* is/are pending in the application.

4a) Of the above claim(s) *14,18,25,26 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,15-17,22-24 and 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/24/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The Amendment filed Nov. 22, 2006, comprising election of invention is acknowledged. Claims 19-20 have been currently cancelled; claim 21 was previously cancelled. Claims 1-18, 23-30 are pending. The elected claims 1-13, 15-17, 22-24 and 27-29 are under examinations. Claims 14, 18, 25-26 and 30 are withdrawn from examiner's consideration as directed to nonelected invention; see 37 CFR1.142 (b).

DETAILED ACTION

Election /Restriction

Applicant's election of Group I, claims 1-13, 15-17, 22-24, 27 in part, and claims 28-29 directed to a human lipase A2 of SEQ ID NO: 9, its encoding DNA of SEQ ID NO: 8 and related subject, and method of assaying inhibitors of SEQ ID NO: 9 and a method of use probes of SEQ ID NO: 8. After reconsideration of claim 27 the examiner includes claim 27 in its entirety to the elected group I.

The election is made with traverse on the ground that lack of unity of invention was not indicated in the International Preliminary Examination Report, although claims 18-20 and 22-30 had not been examined.

Applicants' argument has been fully considered, but is found not persuasive. Firstly, the opinion presented in the International Preliminary Examination Report is not binding for the examiner in the national stage, and, secondly, the Applicants themselves accepted the restriction of Nov. 1, 2006, by marking in the amendment of Nov. 22, 2006 claims 14, 18, 25-26 and 30 as withdrawn. The restriction is proper for the reasons explained in the action of Nov. 1, 2006 and MADE FINAL.

Priority

Applicants claim of benefits of Japanese application 2002-8435 filed Jan. 17, 2002, has been noted. However, the certified copy of the priority document filed in this application is in Japanese, therefore, the examiner is not able to find whether the subject matter of the claims under investigation is presented in full in the Japanese application. Thus, the priority of the instant claims to the Japanese application has not been granted. At present, the claims are entitled to the priority date that is the date of filing of the PCT /JP03/00328, i.e., Jan. 17, 2003.

Objections

Specfication

1. The specification contains a typographical error on page 14, line 20.

2. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors in the specification of which applicant may become aware.

Claims

Claim 1 is objected to because the nucleotide sequence capable hybridizing with a nucleic acid of SEQ ID NO: 8 does not encode itself any phospholipase A2. This is a complementary sequence to the nucleotide sequence capable hybridizing with a nucleic acid of SEQ ID NO: 8 that is likely to have this property.

Claim 13 is objected to for improper English. In step 1) line two "to give a culture" should be deleted. In step 2) line 1 and 2 the phrases "encoded on the recombinant vector" and "obtained in the above step 1" should be deleted.

Claims 6 and 8 are objected to for improper language "having a sequence homology of 70% or more, as compared to a full length", which should be "having 70% or more sequence homology to the full length etc."

Rejections

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-8, 10-13, 15-17 and 22- 24, are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. In the absence of the hand of man, naturally occurring proteins and/or nucleic acids are considered non-statutory subject matter; Diamond v. Chakrabaty, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims to contain wording such as "An isolated and purified protein or nucleic acid". It should be noted that a recombinant enzymes/proteins are assumed to be identical to those produced naturally unless otherwise indicated.

Claims 27-29 are objected to as depending on the rejected claim 1.

35 USC 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-13, 15-17, 22-24 and 27-29, 6, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are directed to, or recite, a DNA that hybridizes with nucleic acid of SEQ ID NO: 8 under "stringent conditions". There are many sets of hybridization conditions in the prior art that are called "stringent" and used for identifying DNA molecules by hybridization. It is noted that Applicants recite stringent hybridization conditions on page 16 line 21 and further, but there is nothing to suggest that other sets of conditions are excluded from the scope of the claims. Including the hybridization conditions in the claims would overcome this rejection.

Claim 13 is rejected for lack of antecedent of the recitation "polypeptide of a phospholipase A_2". There is no sufficient antecedent for this phrase in the claim. The preamble is not reciting recombinant production of phospholipase A2, but **a** polypeptide.

Claim 15 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim is directed to three methods simultaneously, to a method of characterizing, identifying and screening. Furthermore, the claim is indefinite

in reciting "characterizing" that is not defined by the claim or the specification. In addition, the claim is indefinite in recitation "assaying an action", because it is not clear what action is meant and how to perform the assay. In addition, the recitation "to determine inhibition of the phospholipase A2" is lacking an antecedent in the claim. The claim, according to the preamble, is directed to "characterizing, identifying or screening a therapeutic agent for an inflammatory dermal disease" and not to an agent that inhibits phospholipase 2.

Claim 22 is rejected for recitation of "chronic intractable dermal disease" without teaching by the claim or specification what the term "intractable " means. Many dermal diseases can be considered intractable. The indefinite recitation renders the claim indefinite. The claim also seems not to further limit claim 15, because the genus of chronic intractable dermal disease is larger than the genus of inflammatory dermal diseases, as the former includes skin cancer not included in the latter.

Claim 24 is confusing in recitation "a compound which has not been known as an inhibitor for **the** phospholipase A_2 [emphasis added]". This limitation is not a true limitation, because if a compound has been known as the inhibitor of the claimed phospholipase A_2 than there is no point to identify this inhibitor as an inhibitor. If however, a compound was known to be an inhibitor of other phospholipases A_2 it should be tested. In the latter case the phrase should be "a compound which has not been known as an inhibitor for **a** phospholipase A_2".

Claims 27-29 are not clear in recitation "An examination method for psoriasis". Do Applicants mean a "diagnostic method" or something else?

Claim 27 is also not clear in recitation "characterized by assaying". The examiner assumes that Applicants mean "comprising assaying".

35 USC 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written description

Claims 1-13, 15-17, 22-23 and 27-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are rejected as directed to a large and variable genera of polypeptides, and methods of use thereof, wherein the polypeptides are

a) conservative substitution variants of SEQ ID NO: 9,

b) naturally occurring allelic variants of SEQ ID NO: 9,

c) modified polypeptides of SEQ ID NO: 9, wherein one or more amino acids in SEQ ID NO: 9 are deleted substituted and or added,

wherein the polypeptides possess a phospholipase A2 activity.

Regarding genus a) Applicants do not disclose the structure of any polypeptide

that is obtained by conservative substitution of amino acid in SEQ ID NO: 9 and retains the phospholipase A2 activity. Although Applicants claim only conservative substitution, conservative substitution as such may change physical and enzymatic properties of the original polypeptide. Applicants do not teach which substitutions are neutral from the point of view of the phospholipase activity.

Regarding genus b) Applicants fail to disclose any natural allelic variant of SEQ ID NO: 9, thus the structure of such variant is not described.

Similarly, regarding genus c) it is lacking description of structure. Applicants have not provided for the structure of even one polypeptide of genus b), not to speak about an identifying characteristic of the whole claimed genus. The disclosure does not provide teachings regarding substitutions and deletions that are neutral from the point of view of the enzymatic activity of SEQ ID NO: 9.

The claims are also directed to a genus of DNA molecules, and methods of their use, wherein the genus comprises molecules 70%, or more, homologous to the translation region of SEQ ID NO: 8 and encode phospholipase A2. The disclosure is lacking written description of structure of such DNA molecules. The disclosure does not teach which modification within the open reading frame of the DNA of SEQ ID NO: 8 are neutral from the point of view of the activity of the encoded polypeptide.

In addition, claims 15-17 are rejected for lack of sufficient written description of a large genus of inflammatory dermal diseases that are recited by the claims. Applicants teach that phospholipase A2 is overexpressed in some types of psoriasis. Psoriasis,

however, is not a disease which identifies the whole genus of inflammatory dermal diseases.

Claim 15 is specifically rejected because the disclosure fails to teach that an inhibitor of phospholipase A2 is a therapeutic agent for any inflammatory dermal disease, including psoriasis. This is a complete lack of written description.

Claim 22 is rejected for lack of sufficient written description of chronic intractable dermal diseases, which consist a large genus of diseases. The disclosure does not teach which dermal diseases are intractable. The large and variable genus of intractable dermal diseases is not identified by psoriasis the only disease taught by Applicants to have overexpressed phospholipase A2.

Furthermore, claim 27 is rejected because the disclosure does not teach any non-human individual having psoriasis and overexpressing the level of an analog of phospholipase A2.

In conclusion, one skilled in the art is not convinced that Applicants were in possession of the claimed invention at the time the application was filed.

Scope of enablement

Claims 1-13, 15-17, 22-23 and 27-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the human phospholipase A2 of SEQ ID NO: 9, its encoding DNA of SEQ ID NO: 8 and methods of their use, does not reasonably provide enablement for:

a) conservative substitution variants of SEQ ID NO: 9,

b) naturally occurring allelic variants of SEQ ID NO: 9,

c) modified polypeptides of SEQ ID NO: 9, wherein one or more amino acids in SEQ ID NO: 9 are deleted, substituted and or added,

d) DNA molecules that are 70%, or more, homologous to the translation region of SEQ ID NO: 8

wherein the polypeptide possesses a phospholipase A2 activity and DNA molecule is coding said enzyme.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Therefore, to make and use the claimed inventions requires undue experimentation.

Factors to be considered in determining whether undue experimentation is required are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses:

a) any conservative substitution variant of SEQ ID NO: 9,

b) any naturally occurring allelic variant of SEQ ID NO: 9,

c) any modified polypeptide of SEQ ID NO: 9, wherein one or more amino acids in SEQ ID NO: 9 are deleted, substituted and or added,

d) any DNA molecule that is 70%, or more, homologous to the translation region of SEQ ID NO: 8

wherein the polypeptide possesses a phospholipase A2 activity and DNA molecule is coding said enzyme. Furthermore, the invention comprises use of a) through c) for identification of its own inhibitors and use of d) for assaying its expression level in human and non-human samples, wherein overexpression is indicative of psoriasis.

Although the art of constructing polypeptides and DNA molecules encoding them is well developed, and the skills of artisans high, to make and use the claimed invention one skilled in the art is forced to research outside the realm of routine experimentation absent teaching of the structure of the polypeptides/polynucleotides. Although the disclosure teaches explicitly SEQ ID NO: 9 and 8 these two structures do not provide for the structures of the species of extremely large genera of polypeptides and polynucleotides claimed. The reasons are presented in the above rejection for lack of written description.

The art teaches unpredictability of the effects of substitutions, deletions and additions of amino acids/nucleotides in amino acid/nucleotide sequences on the enzymatic activity of a polypeptide. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must

provide a reasonable amount of guidance with respect to the direction in which the modification of SEQ ID NO: 9 and 8 should proceed to obtain products a)-c) and d). As to the product b) one having skills in the art cannot make it because the natural allelic variant cannot has to be isolated and not made. Applicants have isolated only SEQ ID NO:9, but not its allelic variants. Providing SEQ ID NO: 9 is not enabling for making a natural allelic variant for this sequence, which is not predictable. Thus, product b) is completely lacking enablement.

All together, without a further guidance on the part of Applicants regarding the structure of the claimed products the experimentation imposed on skilled artisans has a low probability of success and is extensive and undue.

Claim 15 and 22 are specifically rejected because the disclosure fails to teach that an inhibitor of the claimed phospholipase A2 is a therapeutic agent for any inflammatory dermal disease or any intractable dermal dermal disease. This is lack of enablement, which imposes on the skilled artisan the experimentation regarding a selection, out of many combinations, the combination of an inhibitor and the disease that fulfill the limitations of the claims. The experimentation imposed on one having skills has a low probability of success and is improper and undue.

35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on

sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1-5 and 8-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Song et al. (Molecular Characterization of Cytosolic Phospholipase A_2-β, J. Biol. Chem, 1999, 274, 17063-17067, included in the IDS). Song et al. disclose a phospholipase A_2 that has an amino acid sequence in which one or **more,** i.e., any number, amino acids in the amino acid sequence shown in SEQ ID NO: 9 are deleted, substituted or added; see Fig. 1, page 17064, of the paper and Fig. 2 of the instant application. Song et al, also disclose DNA molecules encoding said polypeptide, expression vetors, host COS cells containing the expression vector, and a recombinant method of production of said phospholipase; see Fig. 1, page 17064 and the paragraph *Expression of cPLA$_2$-β in COS Cells and PLA$_2$ Activity Assay* on page 17065, right column of the paper. Song et al. teach the details of the rejected claims.

Conclusion

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be

obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1652

Patent Examiner

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